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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/848,616	05/04/2001	Peter Sebbel	1700.0180002/JAG/BJD	6018

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EXAMINER
MOSHER, MARY

ART UNIT	PAPER NUMBER
1648	11

DATE MAILED: 02/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/848,616	Applicant(s) Sebbel et al
	Examiner Mosher	Art Unit 1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *5/9/2002, 9/6/2002, 11/27/2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-85* is/are pending in the application.

4a) Of the above, claim(s) *1-27, 32, 33, 39, 40, 45-47, 57-60, 63-77, 81, and* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *28-31, 34-38, 41-44, 48-56, 61, 62, 78-80, and 83-85* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *16*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

Applicant's election without traverse of species 3, Hepatitis B particle with covalently associated antigen, sequence having at least 90% identity to SEQ ID NO:158, in Paper No. 9 is acknowledged. Claims 1-27, 32, 33, 39, 40, 45-47, 57-60, 63-77, 81-82 are therefore withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim, and the remaining claims 28-31, 34-38, 41-44, 48-56, 61, 62, 78-80, 83-85 have been examined to the extent that they read upon the elected species. Election was made without traverse in Paper No. 9.

Claim Objections

Claims 28-30, 34, 36-38, 41-44, 48-56, 61, 62, 78-80, 83-85 are objected to because of the following informalities: These claims read, at least in part, on nonelected species. Appropriate correction is required.

Claims 48-56, 79, 80, and 83-85 are also objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiple dependent claim. See MPEP § 608.01(n). In the interest of compact prosecution, these claims have been treated as if they depend, directly or indirectly, from claim 28. However, this treatment does not relieve applicant of the burden of response to this objection.

Claim Rejections - 35 USC § 112

Claim 34-38, 41-44, 61, 62, and 78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 34 recites the limitation "said core particle", see the next to the last line on page 150. There is insufficient antecedent basis for this limitation in the claim. This affects the dependent claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 28-31, 61, and 62 are rejected under 35 U.S.C. 102(e) as being anticipated by Birkett 6,231,864. Birkett teaches production of hepatitis B core particles modified to contain a chemically reactive amino acid (such as lysine inserted at residue 78), and chemical conjugation of an antigenic determinants to the reactive amino acid by a linker reactive with an amino group and a sulfhydryl group. See examples 1-4 for a working example. Birkett's HBV core sequence is more than 90% identical to SEQ ID NO:158, see attached alignment. Therefore Birkett meets each and every limitation of the claims for the elected species.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 41, 42, 44, 48-56, 79, and 80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Birkett 6,231,864. These claims differ from above in specifying the type of antigenic determinant attached to the HBV core particle, and in specifying use as a vaccine or to induce an immune response. However, Birkett explicitly suggests vaccine use, and suggests many of the listed types of antigenic determinants. See for example Table 2, and columns 21-25. Birkett further expressly suggests inclusion of T cell as well as B cell determinants, see column 22, lines 57 to column 23, line 19. It would have been within the ordinary skill of the art to carry out the

explicit suggestion made in the reference, with reasonable expectation of success. The invention as a whole is therefore prima facie obvious, absent unexpected results.

Claims 34, 35, 37, 41, 42, 44, 48-56, 61, 62, 79, and 80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Birkett 6,231,864 in view of Pasek et al (Nature 282, 575-579, 1979). These claims differ from Birkett in that they specify SEQ ID NO: 158 as the core sequence. As discussed above, Birkett teaches production of hepatitis B core particles modified to contain a chemically reactive amino acid (such as lysine inserted at residue 78), and chemical conjugation of an antigenic determinants to the reactive amino acid. Birkett teaches that the insert carrying the reactive amino acid is preferably 1 to 10 amino acids, see column 4, lines 11-16, and that lysine is the most preferred reactive amino acid, see column 4, lines 29-33. Birkett differs from the claimed invention only in that the core sequence is slightly less than 95% identical to SEQ ID NO:158, see the attached alignment. However, Birkett suggests that a variety of HBV core sequences can be used, see for example column 10, lines 7-21.. Pasek et al teaches a known HBV core sequence, which is identical to SEQ 95 except for a 5-amino acid insert at residue 78, see the attached alignment. Since Birkett suggests that any core sequence can be used, substitution of any known core sequence, such as the sequence of Pasek et al, is seen as obvious. Furthermore, additional modification to use a 5-amino acid insert containing lysine is also seen as obvious, given the teachings in Birkett regarding preferred use of a 1 to 10-amino acid insert. The invention as a whole is therefore prima facie obvious, absent unexpected results.

Claims 43 and 78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Birkett 6,231,864 as applied to claims 41, 42, 44, 48-56, 79, and 80 above, and further in view of Neurath et al 5,565,548. This claim further limits the invention by requiring that the attached immunogenic determinant induce an immune response against an allergen. Birkett teaches that any hapten against which antibody production is desired can be attached to the modified HBV core particle, see column 13, lines 37-40. Birkett does not specifically discuss antibody production against allergens. However, Neurath teaches combination of HBV and allergen immunogens, see for example the Abstract and claims 1-2. Therefore, an immunogenic determinant of an allergen would have been an obvious species to choose within the broad teachings of Birkett. The invention as a whole is therefore prima facie obvious, absent unexpected results.

Claims 36 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Birkett 6,231,864 in view of Pasek et al (Nature 282, 575-579, 1979) as applied to claims 34, 35, 37, 41, 42, 44, 48-56, 61, 62, 79, and 80 above, and further in view of Mark et al 4,959,314 and Zhou et al (Journal of Virology 66(9): 5393-5398, 1992). These claims differ from the above in that they require alteration of one or more cysteine residues in the core sequence. Mark et al teaches deletion or replacement of nonessential cysteines, to eliminate undesirable intramolecular or intermolecular cross linking in a recombinant protein. Zhou et al teaches that all the HBV core protein cysteines are nonessential for assembly of core particles. Therefore, it would have been obvious to delete or replace some or all of the HBV core cysteines, to achieve the advantages

taught by Mark et al, with reasonable expectation of success. The invention as a whole is therefore prima facie obvious, absent unexpected results.

Claims 83-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Birkett 6,231,864 as applied to claims 41, 42, 44, 48-56, 79, and 80 above, and further in view of Davis et al WO 98/40100. These claims further limit the invention in that they specify inducing a Th2 response, without generating a Th1 response. As discussed above, Birkett suggests combination of modified HBV core particles with adjuvants. One of the suggested adjuvants is alum, see column 24, line 1; alum is well-known to be commonly used in human vaccines. Davis et al teaches that the combination of alum with hepatitis B particles leads to a Th2 response, without Th1 response, see page 25. Therefore, for one of ordinary skill in the art wishing to induce a TH2 response, it would have been obvious to choose the alum-adjuvanted embodiment suggested by Birkett, with reasonable expectation of success.

Double Patenting

Claims 28-31, 34-38, 41-44, 48-56, 61, 62, 78-80, 83-85 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 50, 51, 54, 57, 58 of copending Application No. 09/449,631 in view of Pasek et al (Nature 282, 575-579, 1979). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims encompass HBV particles modified by covalent attachment of antigen to a "first attachment site." The copending application

supports the claim with an example 23, which teaches the same "first attachment site" as in SEQ ID NO:158; Pasek et al teaches the rest of SEQ ID NO: 158.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Information Disclosure Statement

The IDS filed 5/9/2002 has been received; however, it appears that all of the cited documents have been lost. Could applicant provide replacement copies?

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is (703) 308-2926. The examiner can normally be reached on Monday -Thursday and alternate Fridays from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is now (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

February 6, 2003

MARY E. MOSHER
PRIMARY EXAMINER
GROUP ~~1800~~ 1600